

## Supplementary Appendix

This appendix has been provided by the authors to give readers additional information about their work.

Supplement to: Tobias DK, Pan A, Jackson CL, et al. Body-mass index and mortality among adults with incident type 2 diabetes. *N Engl J Med* 2014;370:233-44. DOI: 10.1056/NEJMoa1304501

## Supplementary Appendix

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**Table S1.** Cohort-specific and Combined Hazard Ratios (95% CIs) for All-Cause Mortality among Participants with Incident Type 2 Diabetes, according to Body-Mass Index Shortly before Diagnosis of Type 2 Diabetes, Smoking Status and Age Group.\*

	No. of deaths / person-yr	Body-Mass Index Category						P for linear trend
		18.5-22.4	22.5-24.9	25.0-27.4	27.5-29.9	30.0-34.9	≥35.0	
<b>Combined NHS and HPFS<sup>†</sup></b>								
<b>Total participants</b>								
Age at diagnosis <65 years	1804/121,450	1.07 (0.78-1.46)	1.00	1.13 (0.92-1.39)	1.05 (0.85-1.30)	1.36 (1.12-1.64)	1.58 (1.29-1.92)	<0.001
Age at diagnosis ≥65 years	1279/57,632	1.60 (1.20-2.13)	1.00	1.15 (0.94-1.39)	1.17 (0.95-1.43)	1.13 (0.92-1.38)	1.01 (0.78-1.31)	0.13
<b>Never smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	713/54,379	0.98 (0.53-1.79)	1.00	1.17 (0.82-1.66)	1.26 (0.89-1.78)	1.47 (1.07-2.02)	1.76 (1.27-2.45)	<0.001
Age at diagnosis ≥65 years	454/25,567	1.24 (0.74-2.07)	1.00	1.22 (0.86-1.72)	1.29 (0.90-1.85)	1.28 (0.90-1.81)	1.33 (0.89-2.00)	0.04
<b>Ever smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	1083/66,287	1.07 (0.74-1.56)	1.00	1.11 (0.86-1.44)	0.93 (0.71-1.22)	1.25 (0.98-1.59)	1.44 (1.11-1.85)	<0.001
Age at diagnosis ≥65 years	809/31,475	1.89 (1.32-2.71)	1.00	1.14 (0.90-1.46)	1.19 (0.93-1.53)	1.07 (0.82-1.38)	0.95 (0.68-1.34)	0.08
<b>The NHS cohort (women)</b>								
<b>Total participants</b>								
Age at diagnosis <65 years	1537/101,679	1.09 (0.79-1.51)	1.00	1.18 (0.93-1.48)	1.05 (0.83-1.32)	1.34 (1.08-1.65)	1.56 (1.25-1.93)	<0.001
Age at diagnosis ≥65 years	804/43,416	1.73 (1.21-2.45)	1.00	1.12 (0.85-1.47)	0.96 (0.72-1.28)	1.08 (0.83-1.41)	1.17 (0.88-1.56)	0.66
<b>Never smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	615/45,714	0.89 (0.47-1.70)	1.00	1.19 (0.81-1.74)	1.26 (0.86-1.83)	1.33 (0.94-1.88)	1.65 (1.16-2.33)	<0.001
Age at diagnosis ≥65 years	315/20,371	1.05 (0.57-1.92)	1.00	1.11 (0.72-1.70)	0.83 (0.52-1.33)	1.07 (0.70-1.64)	1.23 (0.78-1.94)	0.17
<b>Ever smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	919/55,806	1.14 (0.78-1.68)	1.00	1.14 (0.85-1.53)	0.91 (0.67-1.22)	1.29 (0.99-1.69)	1.46 (1.10-1.92)	<0.001
Age at diagnosis ≥65 years	485/22,929	2.49 (1.59-3.90)	1.00	1.12 (0.78-1.60)	1.09 (0.75-1.58)	1.15 (0.81-1.62)	1.15 (0.78-1.67)	0.71
<b>The HPFS cohort (men)</b>								
<b>Total participants</b>								
Age at diagnosis <65 years	267/19,771	0.86 (0.30-2.47)	1.00	1.02 (0.64-1.60)	1.08 (0.67-1.72)	1.43 (0.93-2.22)	1.72 (1.05-2.83)	0.001
Age at diagnosis ≥65 years	475/14,216	1.38 (0.85-2.25)	1.00	1.18 (0.89-1.54)	1.43 (1.07-1.90)	1.20 (0.87-1.65)	0.53 (0.29-0.96)	0.03
<b>Never smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	98/8665	1.90 (0.33-10.99)	1.00	1.05 (0.44-2.54)	1.25 (0.50-3.08)	2.58 (1.15-5.83)	2.87 (1.14-7.21)	<0.001
Age at diagnosis ≥65 years	139/5196	1.87 (0.72-4.82)	1.00	1.44 (0.81-2.57)	2.43 (1.39-4.26)	1.83 (0.99-3.37)	1.78 (0.73-4.31)	0.07
<b>Ever smokers<sup>‡</sup></b>								
Age at diagnosis <65 years	164/10,481	0.42 (0.10-1.85)	1.00	1.01 (0.58-1.77)	1.04 (0.59-1.83)	1.07 (0.62-2.02)	1.33 (0.71-2.49)	0.10
Age at diagnosis ≥65 years	324/8546	1.15 (0.63-2.10)	1.00	1.17 (0.84-1.61)	1.29 (0.92-1.81)	0.97 (0.66-1.44)	0.40 (0.18-0.92)	0.008

\* The P for interaction was <0.001 for total participants and never smokers in the NHS; the P for interaction was <0.001 for total participants in the HPFS, and 0.52 for never smokers in the HPFS. Data were adjusted for age, race, marital status, menopausal status (the NHS cohort only), family

history of diabetes, smoking status, alcohol intake, and Alternate Health Eating Index dietary score. NHS denotes Nurses' Health Study, and HPFS denotes Health Professionals Follow-up Study.

† The results from the two cohorts were combined by a fixed-effect meta-analysis.

‡ A total of 20 women (7 deaths) and 79 men (17 deaths) with missing data on smoking status were excluded from the stratified analysis.

**Table S2.** Cohort-specific and Combined Hazard Ratios (95% CIs) for All-Cause Mortality among Participants with Incident Type 2 Diabetes, according to Three-Category Body-Mass Index Shortly before Diagnosis of Type 2 Diabetes and Smoking Status.

	Body-Mass Index Category			P for linear trend
	18.5-24.9	25.0-29.9	≥30.0	
Combined NHS and HPFS*				
Total				
Age-adjusted model	1.00	1.01 (0.90-1.13)	1.16 (1.04-1.30)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	1.02 (0.91-1.14)	1.18 (1.05-1.32)	<0.001
Never smokers <sup>‡</sup>				
Age-adjusted model	1.00	1.16 (0.95-1.40)	1.45 (1.20-1.75)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	1.15 (0.94-1.40)	1.40 (1.16-1.70)	<0.001
Ever smokers <sup>‡</sup>				
Age-adjusted model	1.00	0.94 (0.82-1.07)	1.02 (0.89-1.17)	0.02
Multivariable adjusted model <sup>†</sup>	1.00	0.97 (0.84-1.11)	1.06 (0.92-1.22)	0.007
The NHS cohort (women)				
Total				
Age-adjusted model	1.00	0.96 (0.84-1.10)	1.17 (1.03-1.32)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	0.97 (0.85-1.11)	1.18 (1.03-1.34)	<0.001
Never smokers <sup>‡</sup>				
Age-adjusted model	1.00	1.13 (0.90-1.42)	1.37 (1.11-1.70)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	1.11 (0.88-1.39)	1.31 (1.05-1.62)	<0.001
Ever smokers <sup>‡</sup>				
Age-adjusted model	1.00	0.88 (0.74-1.04)	1.07 (0.91-1.25)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	0.90 (0.75-1.06)	1.10 (0.94-1.30)	<0.001
The HPFS cohort (men)				
Total				
Age-adjusted model	1.00	1.11 (0.91-1.34)	1.15 (0.93-1.42)	0.70
Multivariable adjusted model <sup>†</sup>	1.00	1.14 (0.93-1.38)	1.17 (0.94-1.46)	0.70
Never smokers <sup>‡</sup>				
Age-adjusted model	1.00	1.21 (0.84-1.73)	1.73 (1.18-2.53)	<0.001
Multivariable adjusted model <sup>†</sup>	1.00	1.25 (0.85-1.83)	1.78 (1.19-2.65)	<0.001
Ever smokers <sup>‡</sup>				
Age-adjusted model	1.00	1.05 (0.84-1.32)	0.91 (0.70-1.19)	0.09
Multivariable adjusted model <sup>†</sup>	1.00	1.12 (0.89-1.42)	0.95 (0.72-1.25)	0.17

\* The results from the two cohorts were combined by a fixed-effect meta-analysis. NHS denotes Nurses' Health Study, and HPFS denotes Health Professionals Follow-up Study.

† Data were adjusted for age, race, marital status, menopausal status (the NHS cohort only), family history of diabetes, smoking status, alcohol intake, and Alternate Health Eating Index dietary score.

‡ A total of 20 women (7 deaths) and 79 men (17 deaths) with missing data on smoking status were excluded from the stratified analysis.

**Table S3.** Cohort-specific and Combined Hazard Ratios (95% CIs) for All-Cause Mortality among Participants with Incident Type 2 Diabetes, according to Corrected Body-Mass Index Shortly before Diagnosis of Type 2 Diabetes and Smoking Status.\*

	Body-Mass Index Category						P for linear trend
	18.5-22.4	22.5-24.9	25.0-27.4	27.5-29.9	30.0-34.9	≥35.0	
Combined NHS and HPFS <sup>†</sup>							
Total							
Age-adjusted model	1.55 (1.20-2.01)	1.00	1.04 (0.89-1.22)	1.07 (0.92-1.25)	1.17 (1.01-1.35)	1.25 (1.07-1.46)	<0.001
Multivariable adjusted model <sup>‡</sup>	1.39 (1.07-1.80)	1.00	1.06 (0.91-1.24)	1.09 (0.93-1.26)	1.17 (1.01-1.36)	1.25 (1.07-1.47)	<0.001
Never smokers <sup>§</sup>							
Age-adjusted model	1.32 (0.80-2.18)	1.00	0.96 (0.73-1.25)	1.16 (0.90-1.50)	1.31 (1.03-1.66)	1.51 (1.17-1.94)	<0.001
Multivariable adjusted model <sup>‡</sup>	1.25 (0.75-2.08)	1.00	0.97 (0.74-1.27)	1.16 (0.89-1.50)	1.28 (1.00-1.64)	1.45 (1.12-1.88)	<0.001
Ever smokers <sup>§</sup>							
Age-adjusted model	1.65 (1.21-2.25)	1.00	1.09 (0.90-1.32)	1.03 (0.85-1.24)	1.09 (0.91-1.30)	1.14 (0.93-1.39)	0.02
Multivariable adjusted model <sup>‡</sup>	1.40 (1.03-1.92)	1.00	1.11 (0.91-1.34)	1.06 (0.88-1.28)	1.10 (0.91-1.32)	1.16 (0.94-1.42)	0.006
The NHS cohort (women)							
Total							
Number of deaths/person-years	64/3011	149/9359	266/16,493	383/24,369	762/47,635	717/44,229	
Age-adjusted model	1.57 (1.17-2.10)	1.00	1.05 (0.85-1.28)	1.04 (0.86-1.26)	1.14 (0.96-1.36)	1.33 (1.11-1.58)	<0.001
Multivariable adjusted model <sup>‡</sup>	1.43 (1.06-1.92)	1.00	1.06 (0.87-1.30)	1.05 (0.87-1.27)	1.15 (0.96-1.37)	1.33 (1.11-1.59)	<0.001
Never smokers <sup>§</sup>							
Number of deaths/person-years	14/1219	56/4063	103/7809	155/10,893	307/21,947	295/20,154	
Age-adjusted model	0.99 (0.55-1.78)	1.00	0.97 (0.70-1.34)	1.13 (0.83-1.54)	1.18 (0.88-1.56)	1.43 (1.07-1.90)	<0.001
Multivariable adjusted model <sup>‡</sup>	0.99 (0.55-1.79)	1.00	0.95 (0.69-1.32)	1.12 (0.82-1.53)	1.13 (0.84-1.50)	1.35 (1.01-1.81)	<0.001
Ever smokers <sup>§</sup>							
Number of deaths/person-years	49/1782	93/5286	162/8656	227/13,402	453/25,631	420/23,979	
Age-adjusted model	1.83 (1.29-2.59)	1.00	1.12 (0.87-1.44)	0.99 (0.78-1.26)	1.13 (0.90-1.41)	1.28 (1.02-1.60)	<0.001
Multivariable adjusted model <sup>‡</sup>	1.59 (1.12-2.26)	1.00	1.12 (0.86-1.44)	1.00 (0.79-1.28)	1.14 (0.91-1.43)	1.29 (1.02-1.63)	<0.001
The HPFS cohort (men)							
Total							
Number of deaths/person-years	15/441	96/3854	193/8176	189/8456	188/9218	61/3842	
Age-adjusted model	1.51 (0.87-2.60)	1.00	1.05 (0.82-1.34)	1.13 (0.88-1.45)	1.24 (0.97-1.59)	1.05 (0.76-1.45)	0.62
Multivariable adjusted model <sup>‡</sup>	1.24 (0.71-2.16)	1.00	1.06 (0.82-1.36)	1.16 (0.90-1.49)	1.24 (0.96-1.61)	1.04 (0.74-1.46)	0.63
Never smokers <sup>§</sup>							
Number of deaths/person-years	5/158	29/1526	47/3139	56/3290	73/3980	27/1769	
Age-adjusted model	2.88 (1.11-7.47)	1.00	0.96 (0.60-1.52)	1.24 (0.79-1.95)	1.70 (1.09-2.64)	1.83 (1.07-3.15)	<0.001
Multivariable adjusted model <sup>‡</sup>	2.45 (0.89-6.72)	1.00	1.03 (0.63-1.69)	1.26 (0.78-2.05)	1.82 (1.14-2.91)	1.90 (1.08-3.36)	<0.001

**Ever smokers<sup>§</sup>**

Number of deaths/person-years	10/283	66/2186	141/4769	130/4837	109/4995	32/1957	
Age-adjusted model	1.14 (0.58-2.22)	1.00	1.05 (0.78-1.40)	1.08 (0.80-1.46)	1.03 (0.75-1.39)	0.77 (0.51-1.18)	0.09
Multivariable adjusted model <sup>‡</sup>	0.88 (0.44-1.73)	1.00	1.09 (0.81-1.47)	1.16 (0.85-1.58)	1.04 (0.75-1.43)	0.79 (0.51-1.23)	0.17

\* Adjustment equations were estimated using NHANES survey data by sex:  $BMI_{\text{measured}} = 0.63 + 1.01 * BMI_{\text{self-reported}} + 0.0006 * \text{Age}$  for women, and  $BMI_{\text{measured}} = 0.29 + 0.98 * BMI_{\text{self-reported}} + 0.012 * \text{Age}$  for men.

† The results from the two cohorts were combined by a fixed-effect meta-analysis. NHS denotes Nurses' Health Study, and HPFS denotes Health Professionals Follow-up Study.

‡ Data were adjusted for age, race, marital status, menopausal status (the NHS cohort only), family history of diabetes, smoking status, alcohol intake, and Alternate Health Eating Index dietary score.

§ A total of 20 women (7 deaths) and 79 men (17 deaths) with missing data on smoking status were excluded from the stratified analysis.



**Table S4.** Cohort-specific and Combined Hazard Ratios (95% CIs) for Cardiovascular, Cancer, and Other-Cause Mortality among Participants with Incident Type 2 Diabetes, according to Body-Mass Index Shortly before Diagnosis of Type 2 Diabetes and Smoking Status.\*

Incident Type 2 Diabetes, according to Body-Mass Index Category before Diagnosis of Type 2 Diabetes and Smoking Status.								
	No. of outcomes	Body-Mass Index Category						P for linear trend
		18.5-22.4	22.5-24.9	25.0-27.4	27.5-29.9	30.0-34.9	≥35.0	
Combined NHS and HPFS <sup>†</sup>								
CVD mortality								
Total participants	941	1.02 (0.68-1.53)	1.00	1.07 (0.83-1.37)	1.11 (0.86-1.44)	1.28 (1.01-1.63)	1.23 (0.93-1.62)	<0.001
Never smokers	340	0.98 (0.45-2.12)	1.00	1.21 (0.77-1.90)	1.43 (0.91-2.24)	1.57 (1.03-2.40)	1.70 (1.08-2.70)	0.004
Ever smokers	592	1.00 (0.61-1.64)	1.00	1.00 (0.74-1.35)	1.03 (0.76-1.41)	1.16 (0.86-1.56)	1.07 (0.75-1.53)	0.02
Cancer mortality								
Total participants	784	1.51 (1.00-2.28)	1.00	1.25 (0.93-1.67)	1.10 (0.81-1.48)	1.44 (1.09-1.91)	1.33 (0.97-1.82)	0.048
Never smokers	266	0.83 (0.34-2.05)	1.00	1.02 (0.61-1.71)	0.86 (0.50-1.47)	1.29 (0.80-2.07)	1.37 (0.83-2.28)	0.01
Ever smokers	514	1.87 (1.15-3.04)	1.00	1.36 (0.95-1.95)	1.23 (0.85-1.79)	1.51 (1.06-2.15)	1.29 (0.86-1.93)	0.54
Other-cause mortality								
Total participants	1358	1.37 (1.01-1.86)	1.00	1.09 (0.89-1.35)	1.07 (0.86-1.33)	1.07 (0.87-1.32)	1.35 (1.08-1.69)	0.002
Never smokers	561	1.44 (0.86-2.40)	1.00	1.20 (0.85-1.69)	1.30 (0.92-1.84)	1.30 (0.94-1.81)	1.58 (1.11-2.25)	<0.001
Ever smokers	786	1.30 (0.89-1.92)	1.00	1.03 (0.79-1.35)	0.95 (0.72-1.25)	0.94 (0.71-1.24)	1.27 (0.95-1.69)	0.09
The NHS cohort (women)								
CVD mortality								
Total participants	650	1.11 (0.70-1.76)	1.00	1.01 (0.72-1.41)	0.93 (0.66-1.30)	1.12 (0.82-1.52)	1.28 (0.94-1.76)	0.002
Never smokers	260	1.11 (0.48-2.55)	1.00	1.39 (0.81-2.39)	1.21 (0.69-2.11)	1.23 (0.73-2.05)	1.46 (0.86-2.48)	0.16
Ever smokers	387	1.16 (0.67-2.03)	1.00	0.82 (0.53-1.26)	0.81 (0.53-1.24)	1.08 (0.73-1.58)	1.21 (0.81-1.81)	0.005
Cancer mortality								
Total participants	612	1.54 (0.97-2.45)	1.00	1.26 (0.88-1.80)	1.08 (0.75-1.56)	1.51 (1.08-2.11)	1.40 (0.99-1.99)	0.04
Never smokers	211	0.58 (0.19-1.75)	1.00	1.02 (0.55-1.87)	0.84 (0.45-1.58)	1.33 (0.77-2.32)	1.42 (0.80-2.50)	0.01
Ever smokers	401	2.03 (1.19-3.48)	1.00	1.38 (0.88-2.16)	1.22 (0.77-1.92)	1.60 (1.05-2.44)	1.35 (0.86-2.12)	0.65
Other-cause mortality								
Total participants	1079	1.28 (0.90-1.80)	1.00	1.13 (0.88-1.46)	0.98 (0.76-1.28)	1.12 (0.88-1.43)	1.43 (1.12-1.83)	<0.001
Never smokers	459	1.14 (0.64-2.03)	1.00	1.10 (0.74-1.64)	1.07 (0.72-1.60)	1.12 (0.77-1.62)	1.47 (1.00-2.15)	0.004
Ever smokers	616	1.35 (0.87-2.10)	1.00	1.16 (0.83-1.63)	0.91 (0.64-1.29)	1.12 (0.82-1.54)	1.42 (1.02-1.97)	0.005
The HPFS cohort (men)								
CVD mortality								
Total participants	291	0.76 (0.32-1.80)	1.00	1.14 (0.78-1.66)	1.41 (0.96-2.07)	1.60 (1.09-2.36)	1.07 (0.61-1.87)	0.17
Never smokers	80	0.44 (0.05-3.59)	1.00	0.86 (0.37-1.98)	1.96 (0.91-4.20)	2.62 (1.24-5.54)	2.75 (1.08-7.01)	<0.001
Ever smokers	205	0.59 (0.20-1.68)	1.00	1.21 (0.80-1.86)	1.35 (0.86-2.12)	1.29 (0.81-2.06)	0.73 (0.35-1.52)	0.90
Cancer mortality								

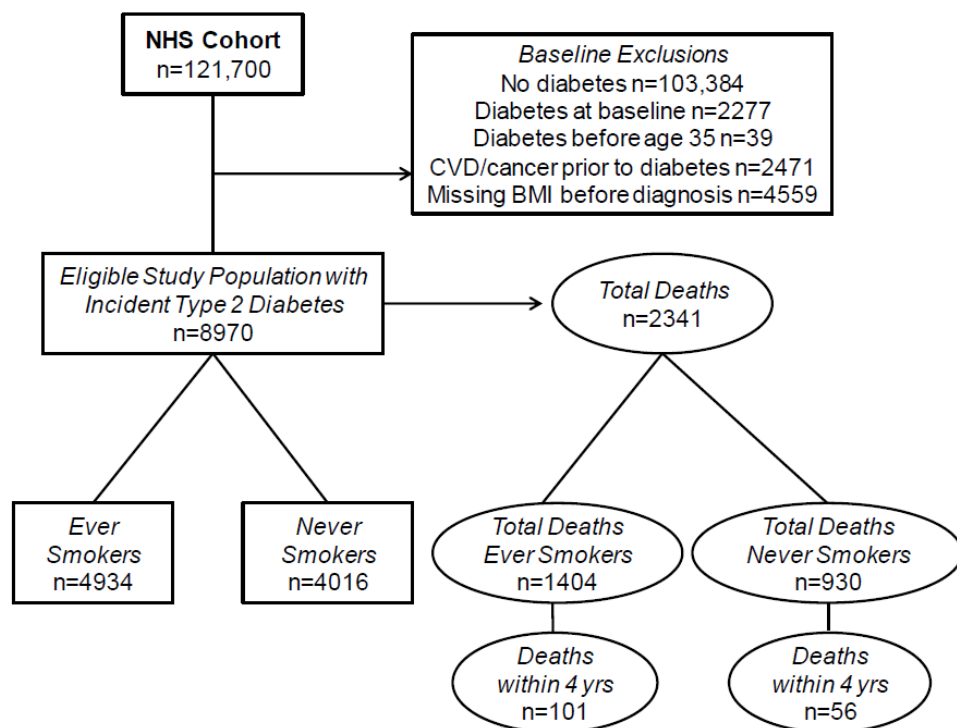
Total participants	172	1.40 (0.57-3.45)	1.00	1.24 (0.75-2.03)	1.13 (0.67-1.91)	1.28 (0.76-2.15)	1.08 (0.53-2.19)	0.84
Never smokers	55	1.74 (0.35-8.52)	1.00	1.04 (0.40-2.69)	0.91 (0.34-2.47)	1.18 (0.47-2.94)	1.22 (0.39-3.79)	0.85
Ever smokers	113	1.32 (0.43-4.01)	1.00	1.33 (0.73-2.41)	1.26 (0.67-2.38)	1.31 (0.68-2.51)	1.04 (0.41-2.62)	0.86
<b>Other-cause mortality</b>								
Total participants	279	1.74 (0.94-3.23)	1.00	1.01 (0.70-1.46)	1.30 (0.89-1.89)	0.94 (0.62-1.42)	1.10 (0.66-1.82)	0.20
Never smokers	102	3.23 (1.10-9.48)	1.00	1.52 (0.77-3.03)	2.36 (1.17-4.77)	2.26 (1.11-4.58)	2.43 (0.99-5.93)	0.04
Ever smokers	170	1.17 (0.53-2.56)	1.00	0.83 (0.53-1.30)	1.02 (0.64-1.61)	0.55 (0.31-0.95)	0.79 (0.41-1.52)	0.02

\* Data were adjusted for age, race, marital status, menopausal status (the NHS cohort only), family history of diabetes, smoking status, alcohol intake, and Alternate Health Eating Index dietary score.

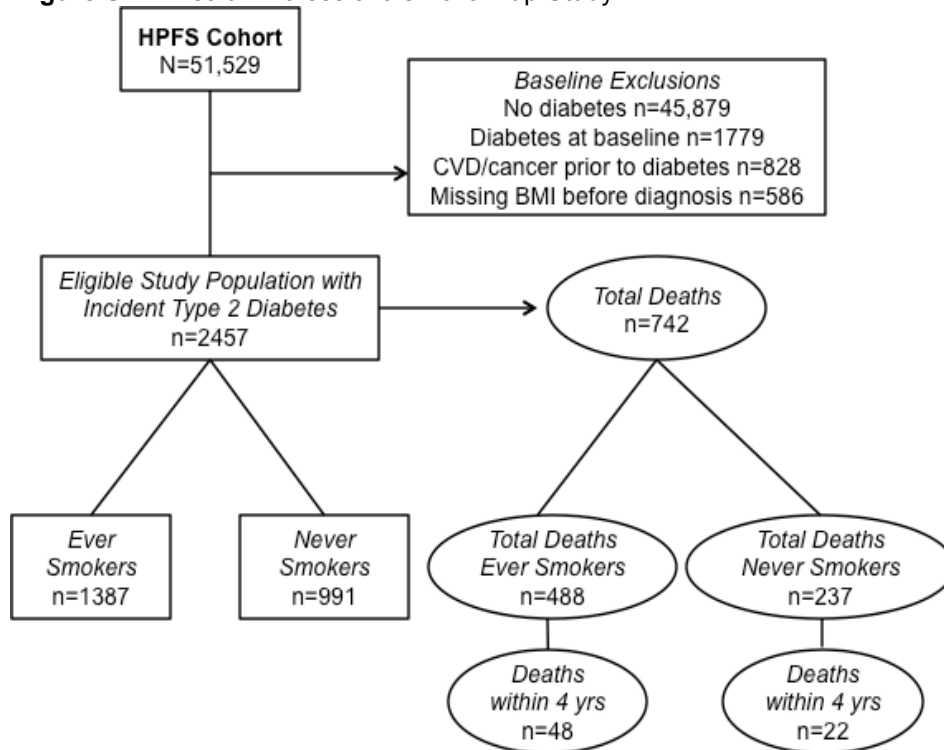
† The results from the two cohorts were combined by a fixed-effect meta-analysis. NHS denotes Nurses' Health Study, and HPFS denotes Health Professionals Follow-up Study.

**Figure S1.** Participant Inclusion and Exclusion Criteria for Nurses' Health Study and Health Professionals Follow-up Study.

**Figure S1A.** Nurses' Health Study



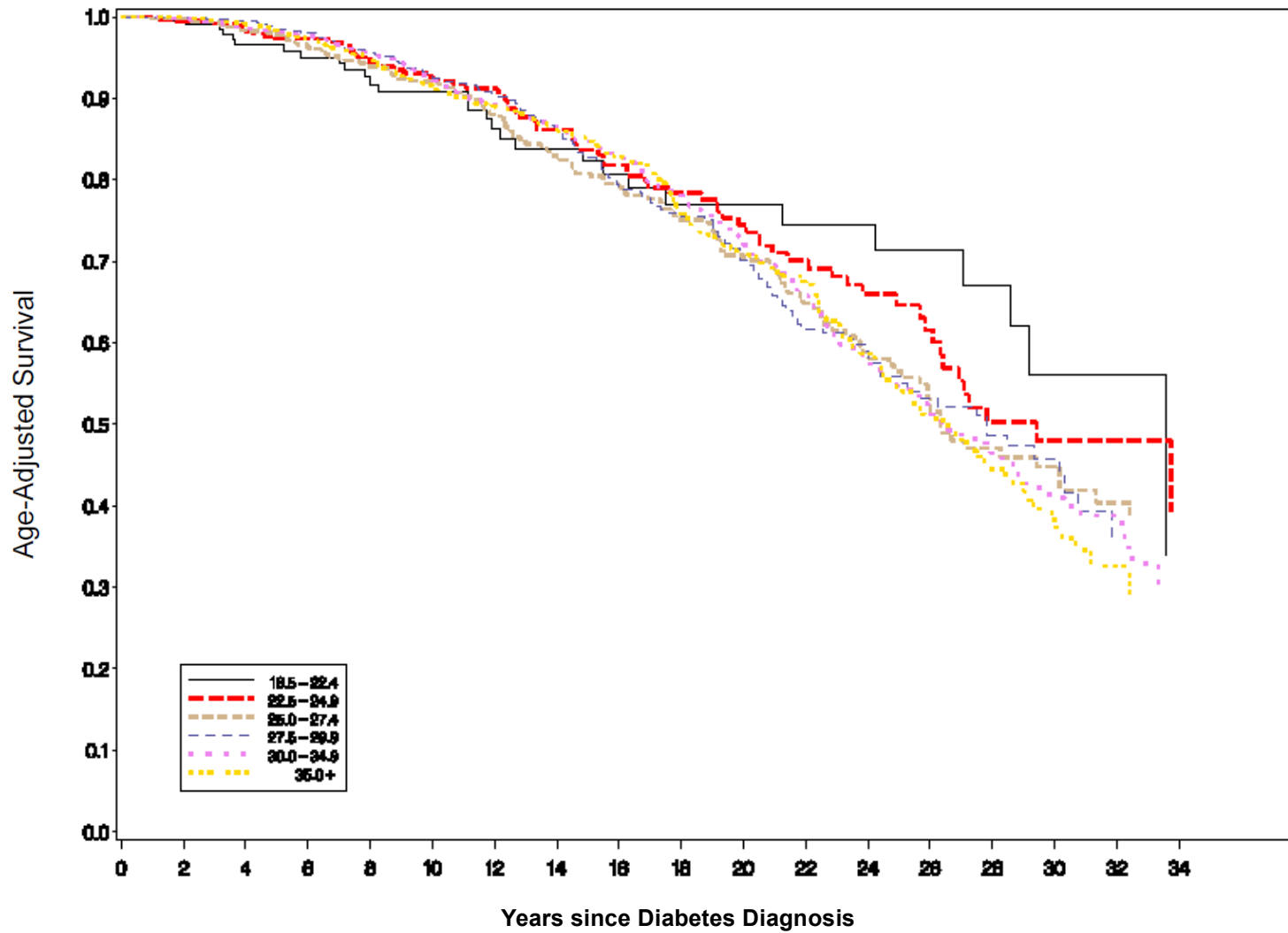
**Figure S1B.** Health Professionals Follow-up Study



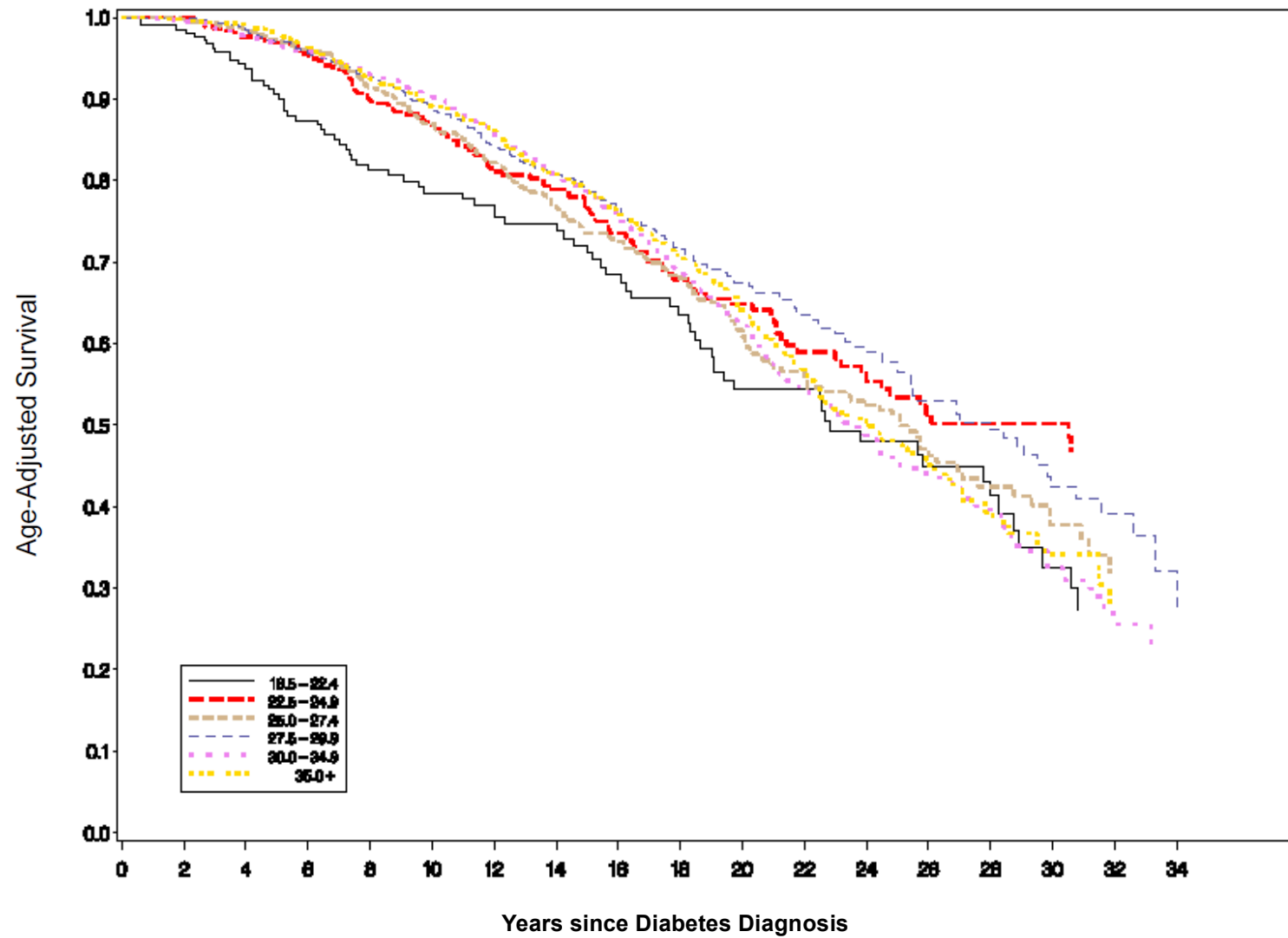
**Figure legend:** A total of 20 women (7 deaths) and 79 men (17 deaths) with missing data on smoking status were excluded from the stratified analysis.

**Figure S2.** Age-Adjusted Survival Curves for All-Cause Mortality According to Body Mass Index Shortly before Diagnosis of Type 2 Diabetes and Smoking Status.

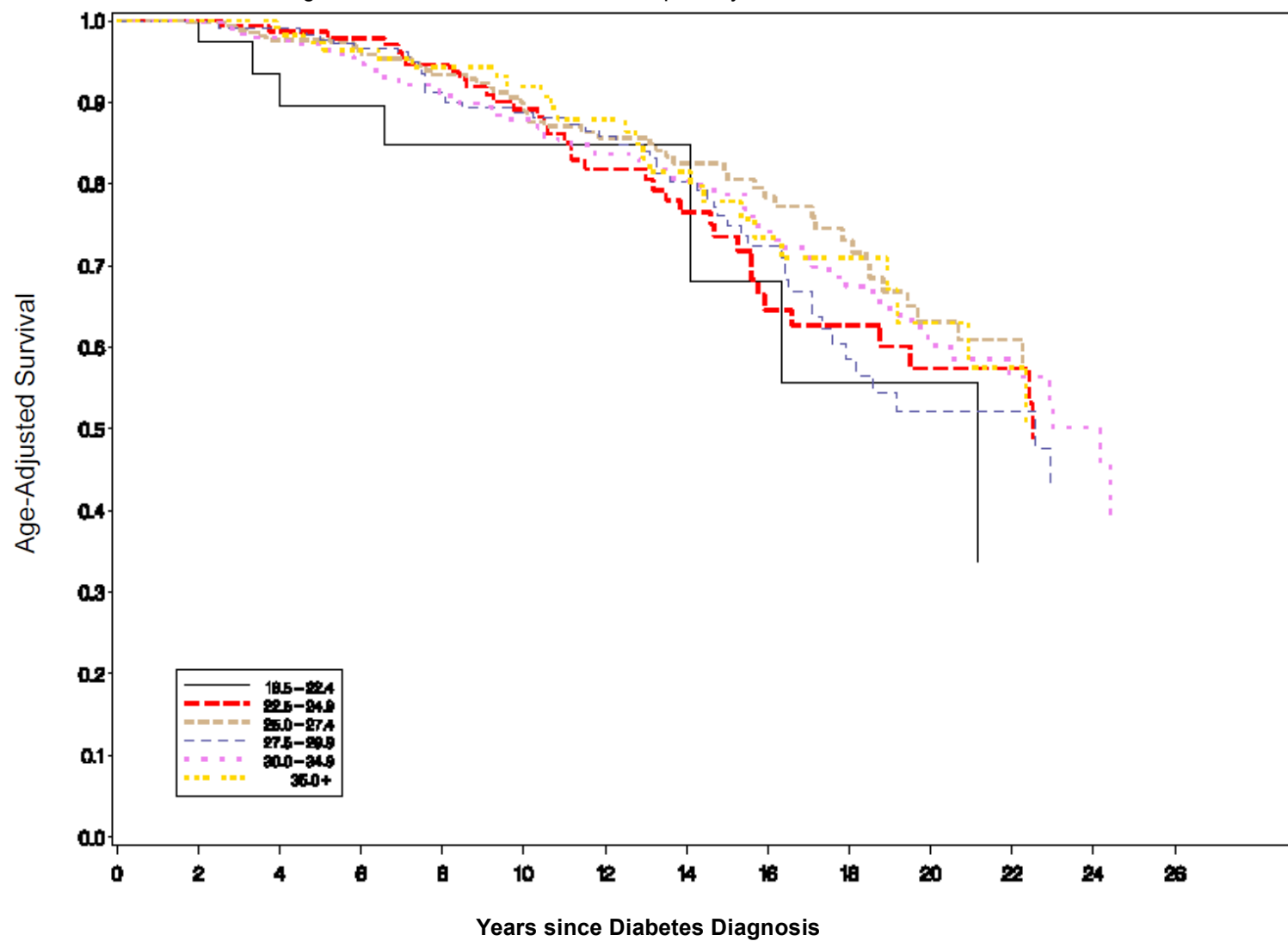
**Figure S2A.** Never Smokers among the Nurses' Health Study



**Figure S2B.** Ever Smokers among the Nurses' Health Study



**Figure S2C.** Never Smokers among the Health Professionals Follow-up Study



**Figure S2D.** Ever Smokers among the Health Professionals Follow-up Study

